of the lithium cation (rather than boron) with the ethereal oxygen atom attached to the β carbon of aldehyde **5** (Cram's cyclic model).[12] Thus, treatment of **6** with *lithium bis(trimethylsilyl)amide*[13] at −78 °C followed by addition of **5** gives rise to the desired diastereoisomer **4**[5] in 88% yield and with a diastereoselection of 17:1, a result highly gratifying in view of the low selectivity (1.5–1.8:1) observed in our earlier boron-mediated condensations.[14] Since ratios ranging from 5–10:1 have been observed for the reactions of **5** with lithium enolates derived from achiral ketones such as 2-methyl-2-(trimethylsiloxy)penta-3-one, the above enhanced stereoselectivity must be due in part to the chirality of the C_8 center of **6**.[4] The synthesis of **4** thus proceeds in 11% overall yield based on (−)-aldehyde **8** and propionaldehyde used.

Lactonization. Desilylation of **4** (CH_3CO_2H–H_2O) yields the dihydroxy ketone **4a** which has been found to exist in equilibrium with the cyclic hemiketal **4b**. The equilibrium between **4a** and **4b** in solution strongly favors the latter and remains virtually unchanged upon preparation of various C_{11}-hydroxy derivatives. Since all attempts to lactonize the mixture of **4a** and **4b** were unsuccessful, it was necessary to make a synthetic detour via the C_9-hydroxy derivative **15**. Reduction of **4** with sodium borohydride gives a 1.4:1 mixture of the 9α- and 9β-hydroxy compounds (**15a,b**), which are separated. The low selectivity at this stage is of no consequence since both isomers are converted to **1** (Scheme III). Bisdichloroacetylation [$(Cl_2CHCO)_2O$, C_5H_5N] of **15a** and **15b** followed by desilylation (CH_3CO_2H) provides epimers **16a,b**, respectively, both of which are most efficiently lactonized with excess copper(I) trifluoromethanesulfonate[15] in benzene containing 2 equiv of diisopropylethylamine to neutralize the strong acid liberated during the reaction. Since the lactone formation proceeds with a delay relative to the disappearance of **16**, the mixed anhydride **17** serves as the probable intermediate in the overall lactonization process. The noticeable difference in the cyclization yield between **16a** and **16b** (41% from **16a** and 23% from **16b**)[16] may well be attributed to the differing conformation of these compounds. After the successful execution of this critical step, the ensuing transformations of **18a,b** via **19a,b** and **20**[5] proceed in a straightforward manner. Removal of the dichloroacetate protecting group (KOH) followed by selective oxidation of the C_9-hydroxy group[17] ($C_5H_5NHCrO_3Cl$, CH_3CO_2Na, CH_2Cl_2) and finally hydrolysis of the acetonide group (CF_3CO_2H, CH_3CN–H_2O) completes the total synthesis of 6-deoxyerythronolide B.

The above synthesis clearly demonstrates two distinct advantages of the aldol approach: (1) simplification of the synthetic design and (2) efficient creation of new chiral centers.

Acknowledgment. We thank Dr. A. O. Geiszler, Abbott Laboratories, for a generous gift of 6-deoxyerythronolide B, and the National Institutes of Health (Grant AI 15403) and Hoffmann-La Roche for generous financial support. D.S.G. is a National Cancer Institute Trainee (NCI Grant 2-T32-CA-09112-01). High-resolution mass spectra were provided by the facility, supported by the National Institute of Health (Grant RR 00317; principal investigator, Professor K. Biemann), from the Biotechnology Resources Branch, Division of Research Resources.

Supplementary Material Available: A listing of spectral data (8 pages). Ordering information is given on any current masthead page.

---

[12] (a) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748. (b) Cram, D. J.; Wilson, D. R. *Ibid.* **1963**, *85*, 1245. (c) For a recent example, see: Collum, D. B.; McDonald, J. H., III; Still, W. C. *Ibid.* **1980**, *102*, 2118. The highest diastereoselection in the aldol reactions utilized in their monensin syntheses is 5:1.

[13] With this amide the (*Z*)-enolates are predominantly generated from ethyl ketones. See also: Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

[14] Masamune, S. *Pure Appl. Chem.*, in press.

[15] Masamune, S.; Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 6756.

[16] When a mixture of **15a** and **15b** was carried through this sequence of reactions, an improved combined yield of **18a** and **18b** was obtained.

[17] Corey, E. J.; Melvin, L. S., Jr. *Tetrahedron Lett.* **1975**, 929.

Tritium Labeling of Organic Compounds by HNaY Zeolite Catalyzed Exchange with Tritiated Water and Their Analysis by ^{3}H NMR

M. A. Long,* J. L. Garnett, and P. G. Williams

School of Chemistry, University of New South Wales
Kensington, N.S.W., Australia

T. Mole

C.S.I.R.O., Division of Material Science
Melbourne, Australia

Received August 27, 1980

The activity of zeolite catalysts is promoted by small amounts of proton donors such as H_2O and HBr[1] (e.g., in alkylation reactions), but deactivation of the catalyst can be expected as H_2O to lattice AlO_4 ratios exceed unity. Thus D_2O is unsuitable as an isotope source for producing highly deuterated organics by zeolite-catalyzed exchange. However, the isotopic abundance typically required in tritium labeled organics, in contrast to the deuterated analogues, is relatively low. We now report that adequately tritiated compounds may indeed be produced very simply by exchange with small amounts of high specific activity tritiated water over HNaY zeolite.

The principle of using small amounts of high activity water in an otherwise "water-sensitive" catalytic system has previously been employed with Lewis acid labeling catalysts.[2,3] The advantages of such procedures include the relative simplicity of handling tritiated water and its low cost compared with alternatives such as tritium gas and tritiated benzene. No vacuum techniques are necessary, and the activity of the product is limited only by the specific activity of the small aliquot of HTO used as isotope source. The reactants, organic (0.1 g), zeolite (25 mg), and tritiated water (5 μL, 40 mCi/mL) were sealed in a glass ampule and heated to 175 °C for the desired reaction time. Products were analyzed by radiogas chromatography and ^{3}H NMR spectroscopy[4] (Table I). Since ^{3}H chemical shifts are yet to be extensively documented,[5] some shift measurements for particular assignments deduced from a consideration of the spectra of compounds labeled by a variety of exchange and synthetic procedures are included in Table I.

The results (Table I) show that the procedure represents a highly efficient method of tritiation of most aromatic compounds. Since the molar ratio of organic compound to water was high, equilibrium represents virtually 100% incorporation of the tritium utilized in the experiment. Only in the case of a severely deactivated aromatic (such as α,α,α-trifluorotoluene) or a bulky molecule (such as triphenylmethane or triphenylsilane) does exchange appear to be substantially hindered. The absence of exchange with bulky molecules is not surprising since the kinetic pore diameter of Y zeolite is ca. 8 Å.

The distribution of tritium within the aromatic nucleus as determined by ^{3}H NMR shows a marked preference toward ortho and para exchange for substituents which are typically ortho–para directing in electrophilic substitution. Similarly, naphthalene and furan exchange predominantly at the α carbon, while the halobenzenes exhibit a preference for para vs. ortho substitution as in nitration and chlorination. Likewise the relative exchange rates of aromatic compounds are similar to those found in common electrophilic substitution reactions, including hydrogen isotope exchange induced by mineral acids. The similarities of zeolite-

---

[1] P. B. Venuto, *Prepr., Div. Pet. Chem., Am. Chem. Soc.*, **16**, B40 (1971).

[2] M. A. Long, J. L. Garnett, and R. F. W. Vining, *J. Chem. Soc., Perkin Trans. 2*, 1298 (1975).

[3] M. A. Long, J. L. Garnett, R. F. W. Vining, and T. Mole, *J. Am. Chem. Soc.*, **94**, 8632 (1972).

[4] M. A. Long, J. L. Garnett, and C. A. Lukey, *Org. Magn. Reson.* **12**, 440, 551 (1979).

[5] J. L. Garnett, M. A. Long, and C. A. Lukey, *J. Chem. Soc., Chem. Commun.*, 634 (1979).

0002-7863/81/1503-1571$01.25/0

Table I. Distribution of Tritium in Representative Compounds Labeled by HNaY Zeolite Catalysis[a, b]

			^{3}H incorp/site, %			
compound	time, h	^{3}H incorp, %	ortho	meta	para	other
PhCH$_3$	1.5	12.5	28.7	<1	42.5	<1 (alkyl)
PhCH$_3$	7	100	29.5	3.3	34.4	<1 (alkyl)
Ph-*n*-C$_7$H$_{15}$	48	22	26.5	2.2	42.5	<1 (alkyl)
PhCH(CH$_3$)$_2$	15	43	7.5	<1	16.2	*c*
PhCH(CH$_3$)CH$_2$CH$_3$	16	74	15.9	2.6	30.9	*d*
PhBr	24[e]	30	13.2	<1	73.6	
PhNH$_2$	74	11	39.5	<1	21.1	
PhOH	73	93	30.2	7.0	25.5	
PhOCH$_3$	2	65	32.2	<1	35.6	<1 (alkyl)
furan	74	62				50 (α), <1 (β)
thiophene	74	100				28 (α), 22 (β)
naphthalene	20	27				22 (α), 2.8 (β)
PhSi(CH$_3$)$_2$H	40	7.6	o,p33	CH$_3$ <1	SiH <1	

[a] Zeolite prepared from Linde SK40 exchange NH_4NO_3 to 3% residual Na and activation to 470 °C. [b] ^{3}H NMR assignments as per literature where available. Other chemical shifts assigned as follows (ppm relative to Me_4Si of pure compound derived as in ref 4). *n*-Heptylbenzene: *o*, 7.04; *m*, 7.14; *p*, 7.06. Isopropylbenzene: *o*, 7.08; *m*, 7.14; *p*, 7.03; CH, 2.55; CH$_3$, 1.09. *sec*-Butylbenzene: *o*, 7.07; *m*, 7.15; *p*, 7.04; CH, 2.40; CH$_2$, 1.46, 1.49; β-CH$_3$, 1.12; γ-CH$_3$, 0.73. Aniline: *o*, 6.35; *m*, 7.05; *p*, 6.69. Phenol: *o*, 7.36; *m*, 7.56; *p*, 7.30. Anisole: *o*, 6.77; *p*, 6.82. Thiophene: α, 7.00; β, 6.88. [c] Alkyltritium (%): CH, <1; CH$_3$, 11.5. [d] Alkyltritium (%): CH, <1; CH$_2$, 6.7; β-CH$_3$, 6.2; γ-CH$_3$, <1. [e] Reaction temperature 195 °C for PhBr.

induced exchange to electrophilic substitution have been reported previously.[6]

No labeling was observed within the alkyl substituent of the straight-chain alkyl aromatics. In branched alkyl aromatics, alkyl exchange was confined to the β-carbon atoms of molecules branched at the α carbon. Such a substitution pattern is expected where exchange involves hydride transfer between the reactant molecule and an α-carbonium ion, as proposed elsewhere.[7,8] Incorporation of tritium into the carbonium ion may take place by deprotonation to an olefinic intermediate and reprotonation.[8,9]

Attempts to label *n*-alkanes by the present procedure were unsuccessful. Branched-chain alkanes on the other hand were in general converted to a range of isomerization products many of which contained tritium. Thus the procedure would appear to be inferior to metal-catalyzed exchange methods[10] for alkanes in general.

The method usefully complements the Lewis acid tritiation procedure[2] where catalysts such as ethylaluminium chloride were utilized again in the presence of small amounts of highly tritiated water as isotope source. The zeolite method has the advantage that the isotope is incorporated with high specificity at sites active toward electrophilic substitution, while the alkylaluminum catalyzed systems yield randomly labeled aromatic centers.[3] Furthermore, the complication of intramolecular substituent shifts, as observed in the Lewis acid tritiation of disubstituted aromatics,[11] such as the bromotoluenes, appears to be absent from the zeolite procedure. Biphenyl formation does not accompany benzene exchange, in contrast to some noble metal exchange methods,[12] nor is there the complication of byproduct formation observed in radiation-induced exchange.[13] Thus the present simple one-step procedure represents a useful method of tritiating a wide range of aromatic and related molecules with high efficiency.

Acknowledgment. We thank the Australian Research Grants Committee and the Australian Institute of Nuclear Sciences and Engineering for their support of the research at the University of New South Wales.

---

(6) P. B. Venuto, E. L. Wu, and J. Cattanach, "Molecular Sieves"; Society of Chemical Industry: London, 1968; p 117.

(7) J. W. Otvos, D. P. Stevenson, C. D. Wagner, and O. Beeck, *J. Am. Chem. Soc.*, **73**, 5741 (1951).

(8) D. P. Stevenson, C. D. Wagner, O. Beeck, and J. W. Otvos, *J. Am. Chem. Soc.*, **74**, 3269 (1952).

(9) T. D. Stewart and W. H. Calkins, *J. Am. Chem. Soc.*, **71**, 4144 (1949).

(10) J. L. Garnett, Proceedings of the 2nd International Conference on Methods of Preparing and Storing Labelled Compounds, Brussels, 1966; pp 709-754.

(11) J. L. Garnett, M. A. Long, R. F. W. Vining, and T. Mole, *Tetrahedron Lett.*, 4075 (1973).

(12) G. E. Calf and J. L. Garnett, *J. Chem. Soc., Chem. Commun.*, 373 (1969).

(13) D. H. T. Fong, C. L. Bodkin, M. A. Long, and J. L. Garnett, *Aust. J. Chem.*, **28**, 1981 (1975).

Synthesis and Characterization of a Nitrosyl, a Nitrido, and an Imido Carbonyl Cluster

Douglas E. Fjare and Wayne L. Gladfelter*

Department of Chemistry, Univeristy of Minnesota
Minneapolis, Minnesota 55455

Received September 9, 1980

Reactions studied in light of the metal cluster-metal surface analogy[1] have concentrated on the reduction of carbon monoxide[2-5] and, to a lesser extent, other unsaturated derivatives, such as nitriles,[6] acetylenes,[7] and olefins.[8] We have discovered and present here some initial results pertinent to two other surface-catalyzed processes: (1) the reaction of carbon monoxide with nitric oxide to produce carbon dioxide and nitrous oxide[9] and (2) the hydrogenation of nitrogen.[10] During our evaluation of the synthesis and properties of nitrosyl carbonyl clusters, we reacted PPN-[$Fe(CO)_3(NO)$][11] [PPN = bis(triphenylphosphin)iminium cation] with $Fe_3(CO)_{12}$ in order to obtain a tetrairon nitrosyl cluster. Instead, X-ray crystallography revealed the presence of the *nitrido*

---

(1) Muetterties, E. L.; Rhodin, T. N.; Band, E.; Brucker, C. F.; Pretzer, W. R. *Chem. Rev.* **1979**, *79*, 91-137.

(2) Bradley, J. S.; Ansell, G. B.; Hill, E. W. *J. Am. Chem. Soc.* **1979**, *101*, 7417-7419.

(3) Bradley, J. S. *J. Am. Chem. Soc.* **1979**, *101*, 7419-7421.

(4) Demitras, G. C.; Muetterties, E. L. *J. Am. Chem. Soc.* **1977**, *99*, 2796-2797.

(5) (a) Tachikawa, M.; Muetterties, E. L. *J. Am. Chem. Soc.* **1980**, *102*, 4541-4542. (b) Beno, M. A.; Williams, J. M.; Tachikawa, M.; Muetterties, E. L. *Ibid.* **1980**, *102*, 4542-4544.

(6) (a) Andrews, M. A.; Kaesz, H. D. *J. Am. Chem. Soc.* **1979**, *101*, 7238-7244. (b) Andrews, M. A.; van Buskirk, G.; Knobler, C. B.; Kaesz, H. D. *Ibid.* **1979**, *101*, 7245-7254. (c) Andrews, M. A.; Kaesz, H. D. *Ibid.* **1979**, *101*, 7255-7259. (d) Andrews, M. A.; Knobler, C. B.; Kaesz, H. D. *Ibid.* **1979**, *101*, 7260-7264.

(7) Thomas, M. G.; Pretzer, W. R.; Beier, B. F.; Hirsekorn, F. J.; Muetterties, E. L. *J. Am. Chem. Soc.* **1977**, *99*, 743-748.

(8) Keister, J. B.; Shapley, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 1056-1057.

(9) Eisenberg, R.; Meyer, C. D. *Acc. Chem. Res.* **1975**, *8*, 26-34.

(10) Emmett, P. H. "The Physical Basis for Heterogeneous Catalysis"; Drauglis, E.; Jaffee, R. I., Eds.; Plenum Press: New York, 1975; pp 3-34.

(11) Connelly, N. G.; Gardner, C. *J. Chem. Soc., Dalton Trans.* **1976**, 1525-1527.